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We thank Scott Kaplan for his interest in our study and his comments. There are two key questions to consider, 1) Is it valid to compare the effect sizes from a meta-analyses of first episode patients to a meta-analysis of chronic patients with schizophrenia? 2) If this is a valid comparison, would one expect to see a significant difference in the effect sizes if progressive changes exist?

1) Vita et al, (2006) compared the results of their meta-analysis of first episode patients to meta-analyses of mainly chronic patients with schizophrenia (Wright, et al. 2000) and conclude that the effect sizes were similar. However comparing the meta-analyses of Vita et al. to Wright et al. is problematic because of the following reasons:

a) The statistical models used to calculate the pooled effect size were different as Wright et al. used a random effects meta-analysis and Vita et al. used a fixed effects meta-analysis.
b) Wright et al. included first episode studies in addition to studies of chronic patients.

To circumvent these problems we have conducted a new meta-analysis of studies measuring the lateral ventricles included in Wright et al, Vita et al and in an additional first episode meta-analysis by Steen et al (2006). We used the same methodology as our previous cross-sectional meta-analysis (Kempton, et al. 2008) and performed a stratified meta-analysis directly comparing the effect size from chronic (n=21 studies, mean duration of illness=12 years) and first episode studies (n=11). There was no significant difference between the effect sizes (p=0.54).

2) We argue that a significant difference would not be expected in the above comparison due to the large increase in inter-study and inter-subject variance associated with meta-analyses of cross-sectional studies. Longitudinal studies remove variance in baseline ventricular volumes and increase statistical power to detect changes over time. Thus a meta-analysis of longitudinal changes is much more sensitive to progressive changes than comparing effect sizes from cross-sectional studies. In conclusion although the comparison between Wright et al and Vita et al is not significant, we can be confident that ventricular dilation is present both in first episode and chronic patients, and that progressive ventricular enlargement occurs in schizophrenia.

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